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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/701,453	04/16/2001	Dan M. Granoff	CHIR-0283	1041

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EXAMINER	
DEVI, SARVAMANGALA J N	
ART UNIT	PAPER NUMBER
1645	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	01/22/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	09/701,453	GRANOFF ET AL.	
	Examiner	Art Unit	
	S. Devi, Ph.D.	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 November 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *17-29* is/are pending in the application.

4a) Of the above claim(s) *29* is/are withdrawn from consideration.

5)☒ Claim(s) *26-28* is/are allowed.

6)☒ Claim(s) *17-25* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

RESPONSE TO APPLICANTS' AMENDMENT

Applicants' Amendment

1) Acknowledgment is made of Applicants' amendment filed 11/01/06 in response to the non-final Office Action mailed 05/01/06. With this, Applicants have amended the claims.

Status of Claims

2) Claims 17 and 26 have been amended via the amendment filed 11/01/06.

Claims 17-29 are pending.

Claims 17-28 are under examination.

Prior Citation of Title 35 Sections

3) The text of those sections of Title 35 U.S. Code not included in this action can be found in a prior Office Action.

Prior Citation of References

4) The references cited or used as prior art in support of one or more rejections in the instant Office Action and not included on an attached form PTO-892 or form PTO-1449 have been previously cited and made of record.

Rejection(s) Withdrawn

5) The rejection of claim 17 made in paragraph 9(a) of the Office Action mailed 05/01/06 under 35 U.S.C § 112, second paragraph, as being indefinite, is withdrawn in light of Applicants' amendment to the claim.

6) The rejection of claim 26 made in paragraph 9(b) of the Office Action mailed 05/01/06 under 35 U.S.C § 112, second paragraph, as being indefinite, is withdrawn in light of Applicants' amendment to the claim.

7) The rejection of claims 18-25, 27 and 28 made in paragraph 9(c) of the Office Action mailed 05/01/06 under 35 U.S.C § 112, second paragraph, as being indefinite, is withdrawn in light of Applicants' amendment to the base claim.

8) The rejection of claims 17-19, 21-23 and 25 made in paragraph 10 of the Office Action mailed 05/01/06 under 35 U.S.C § 103(a) as being unpatentable over Costantino *et al.* (*Vaccine* 10:

691-698, 1992 - already of record) in view of Dalseg *et al.* (*Vaccines* 96. (Ed) Brown F. Cold Spring Harbor Laboratory Press, Cold Spring Harbor, N.Y., pages 177-182, 1996), is withdrawn. A modified rejection is set forth below.

9) The rejection of claims 17-19, 21-23 and 25 made in paragraph 11 of the Office Action mailed 05/01/06 under 35 U.S.C § 103(a) as being unpatentable over Costantino *et al.* (*Vaccine* 10: 691-698, 1992 - already of record) and Dalseg *et al.* (*Vaccines* 96. (Ed) Brown F. Cold Spring Harbor Laboratory Press, Cold Spring Harbor, N.Y., pages 177-182, 1996) in view of Paradiso *et al.* (*Dev. Biol. Stand.* 87: 269-275, 1996 - already of record), is withdrawn. A modified rejection is set forth below.

10) The rejection of claim 24 made in paragraph 12 of the Office Action mailed 05/01/06 under 35 U.S.C § 103(a) as being unpatentable over Costantino *et al.* (*Vaccine* 10: 691-698, 1992 - already of record) as modified by Dalseg *et al.* (*Vaccines* 96. (Ed) Brown F. Cold Spring Harbor Laboratory Press, Cold Spring Harbor, N.Y., pages 177-182, 1996) and Paradiso *et al.* (*Dev. Biol. Stand.* 87: 269-275, 1996 - already of record) as applied to claim 17, and further in view of Seid (US 6,638,513,) ('513), is withdrawn. A modified rejection is set forth below.

Modified Rejection(s)

The modified art rejections set forth below could not have been set forth previously since the applied US patent 7,118,757 was published in October 2006 after the mailing of the previous Office Action in the instant application on 05/01/06.

Rejection(s) under 35 U.S.C § 103

11) Claims 17-19, 21-23 and 25 are rejected under 35 U.S.C § 103(a) as being unpatentable over Costantino *et al.* (*Vaccine* 10: 691-698, 1992 - already of record) in view of Seid Jr. *et al.* (US 7,118,757) ('757).

The reference of Seid Jr. *et al.* ('757) is applied in this rejection because it qualifies as prior art under subsection (e) of 35 U.S.C § 102 and accordingly is not disqualified under U.S.C 103(a).

Costantino *et al.* taught a conjugate vaccine comprising immunologically effective amounts of group C meningococcal oligosaccharides conjugated to CRM 197 and aluminium hydroxide, and a method of inducing an immune response to group C *Neisseria meningitidis* by administering an

immunologically effective amount of the vaccine to a subject (see page 693).

Costantino *et al.* do not teach the use in their conjugate vaccine of outer membrane vesicles from a strain of group B *Neisseria meningitidis*, including the strain 44/76 of group B *Neisseria meningitidis*.

However, Seid Jr. *et al.* ('757) disclosed a vaccine formulation (i.e., immunogenic composition) comprising appropriate concentration of isolated outer membrane vesicles (OMVs) from *Neisseria meningitidis*, including serogroup B *Neisseria meningitidis* strain H44/76 (B:15:P1,7.16), and expressly taught that these OMVs can be used in mixtures, multivalent vaccines, or in conjunction with other antigens of *Neisseria meningitidis,* including oligosaccharide or polysaccharide capsular components of serogroup C *Neisseria meningitidis* with or without conjugation to a protein such as non-toxic mutant CRM197 using standard techniques for coupling saccharides to proteins. Seid Jr. *et al.* ('757) taught that their meningococcal OMV vaccine formulation contains an adjuvant and can advantageously contain preferably meningococcal C capsular polysaccharides covalently coupled to a protein carrier such as a nontoxic CRM mutant, a *Salmonella* flagellin, or a human albumin. See 'Summary of the Invention' in column 2; paragraph bridging columns 3 and 4; Example 1B; first and second full paragraphs in column 10; lines 38-45 in column 4; paragraph bridging columns 10 and 11; Examples 14 and 15; and Table 5B depicting MenC-CRM197 conjugate plus alum. Encompassed within the scope of Seid Jr.'s ('757) meningococcal C capsular polysaccharides and Seid Jr.'s protein carrier respectively are depolymerized meningococcal C capsular polysaccharides, i.e., oligosaccharides (see Examples 10 and 14), and CRM197. See the sentence bridging columns 9 and 10; and Table 5B depicting MenC-CRM197 conjugate plus alum. Via Examples 10 and 14, Seid Jr. *et al.* ('757) taught how to conjugate a serogroup C meningococcal depolymerized capsular polysaccharide (i.e., oligosaccharide) to one of the above-mentioned protein carriers. Seid Jr. *et al.* ('757) further taught that the polysaccharide (meaning meningococcal polysaccharide) vaccine can be enhanced by a vaccine according to their invention as a vaccine with broad, extensive action against most serotypes. Seid Jr. *et al.* ('757) taught that since meningococcal disease is currently caused chiefly by group B meningococci and because the class 1 outer membrane proteins (present in the OMV formulationss) occurring in group B meningococci also occur in group A, C, W-135 and Y

meningococci, the vaccines of their invention should be effective in preventing disease caused by group A, C, W-135 and Y. See first full paragraph in column 4.

Given the express teaching of Seid Jr. *et al.* ('757) that meningococcal OMV formulations can be used in conjunction with other antigens of *Neisseria meningitidis* including oligosaccharide or polysaccharide capsular components of serogroup C *Neisseria meningitidis* conjugated to a protein carrier such as non-toxic mutant CRM197, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to combine Seid Jr.'s ('757) outer membrane vesicle vaccine formulation made from the group B meningococcal reference strain H44/76 with Costantino's group C *Neisseria meningitidis* aluminum hydroxide-containing oligosaccharide-CRM_{197} conjugate vaccine to produce the instant invention, with a reasonable expectation of success. Given the express teaching of Seid Jr. *et al.* ('757) that the class 1 outer membrane proteins present in their group B meningococcal OMV formulations also occur in other groups including groups A, W-135 and Y meningococci, one of ordinary skill in the art would have been motivated to produce the instant invention for the expected benefit of providing a mixed or multivalent vaccine that uses Seid Jr.'s ('757) H44/76 B *Neisseria meningitidis* outer membrane vesicles (OMVs) advantageously in conjunction with a group C *Neisseria meningitidis* oligosaccharide-CRM_{197} conjugate and provides broad, extensive action against most serotypes and is effective in preventing disease caused by group A, C, W-135 and Y as taught by Seid Jr. *et al.* ('757).

Claim 22 is a product-by-process claim which includes the process limitation: 'vesicles are produced by a deoxycholate extraction process'. When claims are drawn to a product-by-process, claims are not limited to the manipulations of the recited step(s), but only the structure implied by the steps. MPEP § 2113 states:

> [E]ven though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process. *In re Thorpe, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985)* (citations omitted).

A product does not have to be made by the same process in order to be the same product, because a product is a product, no matter how it is claimed. Applicants have not shown that the alleged difference(s) in the process results in a product that is structurally different from the product of the

prior art. In the instant case, Applicants have not shown that the underlying structure of the prior art group B meningococcal outer membrane vesicles differs from that of the instantly claimed vesicles.

Claims 17-19, 21-23 and 25 are *prima facie* obvious over the prior art of record.

12) Claim 24 is rejected under 35 U.S.C § 103(a) as being unpatentable over Costantino *et al.* (*Vaccine* 10: 691-698, 1992 - already of record) as modified by Seid Jr. *et al.* (US 7,118,757) ('757) as applied to claim 17 above, and further in view of Seid (US 6,638,513, already of record) ('513).

The reference of Seid ('513) is used in this rejection because it qualifies as prior art under 35 U.S.C § 102(e) and therefore is not disqualified as prior art under 35 U.S.C § 103(a).

The teachings of Costantino *et al.* as modified by Seid Jr. *et al.* ('757) are explained above, which do not teach their composition as further comprising polylactic acids or polyglycolic acids.

However, the use of polylactic acids or polyglycolic acids in combination with a meningococcal oligosaccharide conjugate was well known in the art at the time of the instant invention. For instance, Seid ('513) taught combining carriers, such as, polylactic or polyglycolic acids with meningococcal glycoconjugates for the purpose of primary vaccination wherein carriers do not themselves induce the production of harmful antibodies (see lines 10-18 in column 9).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to add Seid's ('513) polylactic or polyglycolic acid to Costantino's immunogenic composition as modified by Seid Jr. *et al.* ('757) to produce the instant invention, with a reasonable expectation of success. One of ordinary skill in the art would have been motivated to produce the instant invention for the expected benefit of providing Costantino's immunogenic composition as modified by Seid Jr. *et al.* ('757) for primary vaccination without inducing the production of harmful antibodies as taught by Seid ('513).

Claim 24 is *prima facie* obvious over the prior art of record.

Relevant Prior Art

13) The following prior art publication documents that group B meningococcal outer membrane vesicles have been routinely mixed with other microbial antigens in a vaccine with no formulation challenges or difficulties.

- In 1987, Zollinger *et al.* (US 4,707,543) disclosed the routine combining of serogroup B *Neisseria meningitidis* outer membrane proteins with a tetravalent vaccine mixture

of meningococcal capsular polysaccharides from serogroups A, C, Y and W-135. The outer membrane proteins used in the multivalent vaccine was obtained from serogroup B *Neisseria meningitidis* strain 44/76 (B:15:P1.16:L3,8) using deoxycholate extraction process. The multivalent vaccine induced high levels of bactericidal antibodies against serogroup B *Neisseria meningitidis*. See Examples; paragraph bridging columns 13 and 14; column 14; and Tables in columns 11 and 12.

Remarks

14) Claims 17-25 stand rejected. Claims 26-28 are allowable.

15) Papers related to this application may be submitted to Group 1600, AU 1645 by facsimile transmission. The Fax number for submission of amendments, responses or papers is (571) 273-8300, which receives transmissions 24 hours a day and 7 days a week.

16) Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAG or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.Mov. Should you have questions on access to the Private PAA system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

17) Any inquiry concerning this communication or earlier communications from the Examiner should be directed to S. Devi, Ph.D., whose telephone number is (571) 272-0854. A message may be left on the Examiner's voice mail system. The Examiner can normally be reached on Monday to Friday from 7.15 a.m. to 4.15 p.m. except one day each bi-week, which would be disclosed on the Examiner's voice mail system.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Jeffrey Siew, can be reached on (571) 272-0787.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (571) 272-1600.

January 2007

S. DEVI, PH.D.
PRIMARY EXAMINER